CLAIMS:

1. A *cis*-acting nucleotide sequence which is capable of rendering the removal of intron/s from a precursor transcript encoded by a gene, which gene harbors at least one such *cis*-acting nucleotide sequence, occurring during the production of mRNA of said gene, dependent upon activation of a *trans*-acting factor, said *trans*-acting factor being an RNA-activated protein kinase which is capable of phosphorylating the α-subunit of eukaryotic initiation factor 2.

2. A *cis*-acting nucleotide sequence according to claim 1 wherein said *trans*-acting factor is the RNA-activated protein kinase (PKR).

3. A *cis*-acting nucleotide sequence according to claim 1 or claim 2 derived from the 3' untranslated region of the human tumor necrosis factor α gene (TNF-α 3'-UTR).

4. A *cis*-acting nucleotide sequence according to any one of claims 1 to 3 which comprises:

   a) the nucleotide sequence substantially as denoted by SEQ ID NO:1; or

   b) biologically functional fragments, derivatives, mutants and homologues of the nucleotide sequence substantially as denoted by SEQ ID NO:1; or

   c) a nucleotide sequence whose complementary nucleotide sequence hybridizes, under conditions which allow for such hybridization to occur, with the nucleotide sequences of (a) or (b).

5. A *cis*-acting nucleotide sequence according to claim 4 which comprises:

   a) the nucleotide sequence substantially as denoted by SEQ ID NO:2; or

   b) biologically functional fragments, derivatives, mutants and homologues of the nucleotide sequence substantially as denoted by SEQ ID NO:2; or

   c) a nucleotide sequence whose complementary nucleotide sequence hybridizes, under conditions which allow for such hybridization to occur, with the nucleotide sequences of (a) or (b).

6. A *cis*-acting nucleotide sequence according to any one of claims 1 to 5 wherein said gene encodes a protein is selected from the group consisting of enzymes, hormones, growth factors, cytokines, structural proteins and industrially or agriculturally applicable proteins, or is itself a therapeutic product, an agricultural product, or an industrially applicable product.

7. A DNA construct comprising:-

- a gene which contains at least one intron;
- a *cis*-acting nucleotide sequence which is capable of rendering the removal of intron/s from a precursor transcript encoded by said gene, which gene includes at least one such *cis*-acting nucleotide sequence, occurring during the production of mRNA of said gene, dependent upon activation of a *trans*-acting factor, said *trans*-acting factor being an RNA-activated protein kinase which is capable of phosphorylating the α-subunit of eukaryotic initiation factor 2, operably linked to said gene; and
- optionally further comprising additional control, promoting and/or regulatory elements.

8. A DNA construct according to claim 7 wherein said *cis*-acting nucleotide sequence comprises:

a) the nucleotide sequence substantially as denoted by SEQ ID NO:1; or

b) biologically functional fragments, derivatives, mutants and homologues of the nucleotide sequence substantially as denoted by SEQ ID NO:1; or

c) a nucleotide sequence whose complementary sequence hybridizes, under conditions which allow for such hybridization to occur, with the nucleotide sequences of (a) or (b).

9. A DNA construct according to claim 7 wherein said *cis*-acting nucleotide sequence comprises:

a) the nucleotide sequence substantially as denoted by SEQ ID NO:2; or

b) biologically functional fragments, derivatives, mutants and homologues of the nucleotide sequence substantially as denoted by SEQ ID NO:2; or

c) a nucleotide sequence whose complementary sequence hybridizes, under conditions which allow for such hybridization to occur, with the nucleotide sequences of (a) or (b).

10. A DNA construct according to any one of claims 7 to 9 wherein said control, promoting and/or regulatory elements are suitable transcription promoters, transcription enhancers and mRNA destabilizing elements.

11. A DNA construct according to claim 7, wherein said gene encodes a protein is selected from the group consisting of enzymes, hormones, growth factors, cytokines, structural proteins and industrially or agriculturally applicable proteins, or is itself a therapeutic product, an agricultural product, or an industrially applicable product.

12. A DNA construct according to any one of claims 7 to 11 wherein said nucleotide sequence is contained within an exon of said gene.

13. A DNA construct according to any one of claims 7 to 11 wherein said nucleotide sequence is contained within an intron of said gene.

14. A DNA construct according to any one of claims 7 to 13 wherein said gene is the human TNF-α gene.

15. A DNA construct according to claim 14 being the plasmid pTNF-α, in which said *cis*-acting element is contained within an exon of the human TNF-α gene.

16. A DNA construct according to claim 15 being the plasmid pTNF-α(3'UTR-α EP).

17. An expression vector according to any one of claims 7 to 13 wherein said gene is the human TNF-β gene.

18. A DNA construct according to claim 17 in which said *cis*-acting element is contained within an exon of the human TNF-β gene.

19. A DNA construct according to claim 18 being the plasmid pTNF-β(3'UTR-α).

20. A DNA construct according to claim 18 being the plasmid pTNF-β(3'UTR-α EP).

21. A DNA construct according to claim 14 in which said gene is the human TNF-α gene and said *cis*-acting element is contained within an intron of said gene.

22. A DNA construct according to claim 21 being the plasmid pTNFα(Δ3'UTR)i3EP.

23. A vector comprising a *cis*-acting nucleotide sequence according to any one of claims 1 to 6 or a DNA construct according to any one of claims 7 to 22 and a suitable DNA carrier, capable of transfecting a host cell with said *cis*-acting nucleotide sequence.

24. A vector according to claim 23 optionally further comprising additional expression, control, promoting and/or regulatory elements operably linked thereto.

25. A vector according to claim 24 wherein said carrier is salmon sperm DNA.

26. A vector according to claim 24 wherein said carrier is viral DNA.

27. A host cell transfected with a DNA construct according to any one of claims 7 to 22.

28. A host cell transfected with a vector according to claim 23.

29. A host cell according to claim 27 or 28 being a eukaryotic or yeast cell.

30. A host cell according to claim 29 being a mammalian hemopoietic cell, fibroblast, epithelial cell, or lymphocyte.

31. A host cell according to claim 27 wherein said eukaryotic cell is the baby hamster kidney (BHK-21) cell line or the Chinese hamster ovary (CHO) cell line.

32. A transgenic animal carrying in its genome a DNA construct according to any one of claims 7 to 22, said transgenic animal being capable of expressing substantial amounts of said gene.

33. A transgenic animal transformed with an expression vector according to claim 23, said transgenic animal being capable of expressing substantial amounts of said gene.

34. A method of regulating gene expression at the mRNA splicing level comprising the steps of:

a) providing a *cis*-acting nucleotide sequence which is capable of rendering the removal of intron/s from a precursor transcript encoded by a gene which contains at least one intron dependent upon activation of a *trans*-acting factor, said *trans*-acting factor being an RNA-activated protein kinase which is capable of phosphorylating the α-subunit of eukaryotic initiation factor 2;

b) operably linking said *cis*-acting nucleotide sequence to said gene to give a DNA construct;

c) optionally linking to the construct obtained in step (b) additional expression control, promoting and/or regulatory elements to give an expression vector;

d) transforming a host cell with the DNA construct obtained in (b) or with the expression vector obtained in (c), said host cell being capable of expressing an RNA-activated protein kinase which is capable of phosphorylating the α-subunit of eukaryotic initiation factor 2, to give a transformed host cell capable of expressing said gene in substantial

amounts, wherein the expression and/or activity of the RNA-activated eIF2αkinase in said host cell is modulated.

35. A method according to claim 34 wherein the activity of the RNA-activated eIF2 αkinase in said host cell is modulated by use of 2-aminopurine or other adenine derivatives.

36. A method according to claim 34 wherein the activation of the RNA-activated eIF2α kinase in said host cell is modulated by use of a transdominant negative mutant of PKRΔ6.

37. A method according to claim 34 wherein the activation of the RNA-activated eIF2αkinase in said host cell is chemically modulated.

38. A method according to claim 37 wherein said modulation is effected by Ca^{2+} ions.

39. A method according to claim 34 wherein the activity of the RNA-activated eIF2α kinase in said host cell is modulated by use of a vector expressing viral proteins.

40. A method according to claim 39 wherein said vector is vaccinia E3L protein or vaccinia K3L protein.

41. A method according to claim 34 wherein the activity of the RNA-activated eIF2α kinase in said host cell is modulated by use of a vector expressing viral RNA.

42. A method according to claim 41 wherein said vector is an.adenovirus VA RNA or the.Epstein-Barr virus Eber RNA.

43. A method for *ex vivo* treating an individual suffering an acquired or hereditary pathological disorder in which a therapeutic product is not made by said

individual, or made is in abnormally low amounts or in a defective form or is made in essentially normal amount to be increased comprising:

a) providing a DNA construct according to any one of claim 7 to 22 or an expression vector according to any one of claims 23 to 26 wherein said gene encodes said therapeutic product;

b) obtaining cells from an individual suffering said disorder and optionally culturing said cells under suitable conditions;

c) transfecting the cells obtained in (b) with a DNA construct or expression vector provided in (a); and

d) re-introducing said cells obtained in (c) into said individual.

44. A method of *ex vivo* treating an individual suffering from a pathological disorder requiring increase of expression of a therapeutic product normally made by said individual in physiological amount comprising:

a) providing DNA construct according to any one of claims 7 to 22 or an expression vector according to any one of claims 23 to 26, wherein said gene encodes said therapeutic product;

b) obtaining cells from an individual suffering said disorder and optionally culturing said cells under suitable conditions;

c) transfecting the cells obtained in (b) with a DNA construct or expression vector provided in (a); and

d) re-introducing said cells obtained in (c) into said individual.

45. A method of providing a therapeutic protein product to a mammal comprising administering to the mammal a DNA construct according to any one of claims 7 to 22, wherein said gene encodes said therapeutic protein product.

46. A method of providing a therapeutic protein product to a mammal comprising administering to the mammal a therapeutically effective amount of transformed

host cells according to any one of claims 27 to 31, wherein said gene encodes said therapeutic protein product.

47. A pharmaceutical composition comprising as active ingredient a therapeutically effective amount of expression vectors according to any one of claims 23 to 26 or of transformed host cells according to any one of claims 27 to 31.

48. A method of producing a recombinant therapeutic or industrially or agriculturally applicable protein comprising the steps of:

a) providing a DNA construct according to any one of claim 7 to 26 or an expression vector according to any one of claims 23 to 26 wherein said gene encodes said protein;

b) transfecting a host cell with a DNA construct or expression vector provided in (a) to give a host cell capable of expressing said protein in substantial amount; and

c) culturing cells obtained in (b) under suitable culture conditions; and

d) isolating said protein from the cell culture obtained in (c).

49. A method of producing a recombinant therapeutic or industrially or agriculturally applicable protein comprising the steps of:

a) providing host cells transfected with a DNA construct according to any one of claim 7 to 22 or an expression vector according to any one of claims 23 to 26 wherein said gene encodes said protein, which are capable of expressing said protein in substantial amount;

b) culturing cells provided in (a) under suitable culture conditions; and

c) isolating said protein from the cell culture obtained in (b).

50. A method of producing a recombinant enzyme, hormone, growth factor, cytokine, structural protein or another industrially or agriculturally applicable protein, comprising the steps of-

a) providing a transgenic animal transformed with a DNA construct according to any one of claims 7 to 22, wherein said gene encodes an enzyme, a hormone, a growth factor, a cytokine, a structural protein or an industrially or agriculturally applicable protein, said transformed animal being capable of expressing said gene in substantial amounts;

b) growing the transgenic animal provided in (a) under suitable conditions to allow the said gene to be expressed; and

c) isolating the protein encoded by said gene from said animal, or from an egg or body secretion thereof.